

09/581,772

Set	Items	Description
S1	306	AU="O'HAGAN D" OR AU="O'HAGAN D." OR AU="O'HAGAN DEREK" OR AU="O'HAGAN DEREK T"
S2	2	AU="O'HAGAN DEREK THOMAS"
S3	7672	AU="SINGH M"
S4	1575	AU="SINGH M."
S5	865	AU="OTT G"
S6	236	AU="OTT G."
S7	33	AU="OTT GARY"
S8	21	AU="BARACKMAN J" OR AU="BARACKMAN JOHN"
S9	53	AU="KAZZAZ J" OR AU="KAZZAZ J." OR AU="KAZZAZ JINA"
S10	10589	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9
S11	37650	MICROPARTICLE? ?
S12	170	S10 AND S11
S13	9487	POLY(5N) HYDROXY (W) ACID
S14	1088	POLYHYDROXY (W) BUTYRIC (W) ACID
S15	18948	POLYCAPROLACTONE
S16	717	POLYORTHOESTER
S17	3760	POLYANHYDRIDE
S18	594	POLYCYANOACRYLATE
S19	6632	POLY(2N) L (W) LACTIDE
S20	14706	POLY(5N) LACTIDE
S21	7571	POLY(5N) LACTIDE(5N) GLYCOLIDE
S22	33111	S13 OR S14 OR S15 OR S16 OR S17 OR S18
S23	14870	S19 OR S20 OR S21
S24	72	S12 AND (S22 OR S23)
S25	27	S24 NOT PY>1997
S26	15	RD (unique items)
S27	1375	S11 AND S22
S28	360	S27 NOT PY>1997
S29	358	RD (unique items)
S30	2161	S11 AND S23
S31	742	S30 NOT PY>1997
S32	467	RD (unique items)
S33	90648	POLYNUCLEOTIDE? ?
S34	728158	NUCLEIC (W) ACID
S35	3736447	DNA
S36	4089743	S33 OR S34 OR S35
S37	604	S11 AND S30 AND S36
S38	101	S37 AND S32
S39	101	RD (unique items)
S40	366065	ADJUVANT? ?
S41	39	S39 AND S40
S42	2161	S30 OR S32
S43	604	S42 AND S36
S44	0	S HUMAN (W) IMMUNODEFICIENCY (W) VIRUS
S45	634832	HIV
S46	634682	S44 OR S45
S47	35438	GP120
S48	5909	GP(W)120
S49	638560	S46 OR S47
S50	1711	GP(W)160
S51	9432	GP160
S52	1226	P24 (W) GAG
S53	796	P24GAG
S54	356	P55 (W) GAG
S55	185	P55GAG
S56	222	S43 AND S46
S57	640347	S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55
S58	14	S6 AND S57
S59	3	S58 NOT PY>1997
S60	30	S56 NOT PY>1997
S61	29	RD (unique items)
S62	554	S42 AND S40
S63	0	ALUMINU,

09/581,772

S64 1828287 ALUMINUM  
S65 198 S62 AND S64  
S66 175 S62(S) S64  
S67 14 S66 NOT PY>1996  
S68 14 RD (unique items)  
S69 105140 S57 AND S46 AND S36  
S70 1764 S11 AND S69  
S71 296 S70 AND (S47 OR S48)  
S72 66 S71 NOT PY>1997  
S73 65 RD (unique items)  
S74 2671 HEXADECYLTRIMETHYLAMMONIUM (W) BROMIDE  
S75 170943 SODIUM (W) DODECYL (W) (SULFATE OR SULPHATE)  
S76 8 S42 AND S74  
S77 83 S42 AND S75  
S78 3 S76 AND S77  
S79 13 S11 AND S40 AND S74  
S80 5 S79 NOT S76  
S81 0 S39 AND S74  
S82 117 S40 AND S74  
S83 38 S11 AND S74  
S84 1172 S11 AND S75  
S85 20 S83 AND S84  
S86 10 S85 NOT PY>1997  
S87 10 RD (unique items)  
S88 18 S83 NOT S85  
S89 4 S88 NOT PY>1997  
S90 4 RD (unique items)  
S91 83 S75 AND S42  
?

26/3,AB/2 / (Item 2 from file: 155)  
DIALOG(R) File 155: MEDLINE(R)

09163368 97166574 PMID: 9014294

**Synthetic peptides entrapped in microparticles can elicit cytotoxic T cell activity.**

Nixon DF; Hioe C; Chen PD; Bian Z; Kuebler P; Li ML; Qiu H; Li XM; Singh M; Richardson J; McGee P; Zamb T; Koff W; Wang CY; O'Hagan D  
United Biomedical Inc., Hauppauge, NY 11788, USA.  
Vaccine (ENGLAND) Nov 1996, 14 (16) p1523-30, ISSN 0264-410X

Journal Code: X60

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Peptides from Plasmodium berghei circumsporozoite protein (CS) and influenza A virus nucleoprotein (NP) were entrapped in **microparticles** prepared from poly ( lactide -co- glycolide ) polymers, and the **microparticles** were administered parenterally to mice. After immunization with single or multiple doses, splenocytes were tested for a cytotoxic T cell (CTL) response and high levels of CTL activity were detected. The CTL induced were CD8+, MHC class I restricted, and could recognize virus infected cells. Peptide entrapped in **microparticles** of mean size < 500 nm were better inducers of CTL than larger **microparticles** (mean > 2 microns and above). **Microparticles** could also be used to deliver lipid modified peptides (lipopeptides) and elicited higher levels of cytolytic activity than either free peptide in **microparticles** or lipopeptide alone. **Microparticles** provide a novel way of inducing a CTL response using synthetic peptides.

26/3,AB/3 (Item 3 from file: 155)  
DIALOG(R) File 155: MEDLINE(R)

08711252 96164474 PMID: 8578845

**Synthetic delivery system for tuberculosis vaccines: immunological evaluation of the M. tuberculosis 38 kDa protein entrapped in biodegradable PLG microparticles .**

Vordermeier HM; Coombes AG; Jenkins P; McGee JP; O'Hagan DT; Davis SS; Singh M

MRC Clinical Sciences Centre, Hammersmith Hospital, London, UK.

Vaccine (ENGLAND) Nov 1995, 13 (16) p1576-82, ISSN 0264-410X

Journal Code: X60

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Tuberculosis remains a major public health burden which could be ameliorated by effective and well-defined subunit vaccines, particularly because the protective efficacy of current M. bovis BCG vaccines is both unpredictable and variable. The immunodominant 38 kDa antigen from Mycobacterium tuberculosis was entrapped in biodegradable poly (DL-lactide co-glycolide) (PLG) **microparticles** which served as a delivery system. Both cellular and humoral immune responses were assessed and compared with those obtained after immunization with the 38 kDa protein emulsified in incomplete Freund's adjuvant (IFA). Vaccination of mice with a single dose of antigen-loaded **microparticles** resulted in specific IgG titres peaking after five weeks comparable to those achieved after vaccination with protein emulsified in incomplete Freund's adjuvant (IFA). T-cell responses were found to be superior to those induced with antigen/IFA. The T- and B-cell epitope specificities ad judged with synthetic peptides were identical following immunization with antigen in **microparticles** or IFA. Differences in adjuvanticity were revealed by measuring antigen-specific IgG1, IgG2a and antigen-induced IFN-gamma secretion in vitro: substantially higher titres of IgG2a were observed following immunization with antigen/ **microparticles** than with 38 kDa protein/IFA. This was paralleled by a tenfold higher secretion of IFN-gamma

in mice injected with antigen/ **microparticles** . Reduction in colony-forming units was not consistent in mice immunized with 38 kDa protein entrapped in **microparticles** which were subsequently infected with live tubercle bacilli. Taken together these results indicate that biodegradable PLG **microparticles** constitute a favorable candidate vaccine delivery system worthy of further assessment in the quest to develop better and defined agents protecting against tuberculosis.

26/3,AB/4 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10840664 BIOSIS NO.: 199799461809  
**Recent advances in vaccine adjuvants: The development of MF59 emulsion and polymeric microparticles .**  
AUTHOR: O'Hagan Derek T ; Ott Gary S; Van Nest Gary  
AUTHOR ADDRESS: Chiron Corp., 4560 Horton St., Emeryville, CA 94704\*\*USA  
JOURNAL: Molecular Medicine Today 3 (2):p69-75 1997  
ISSN: 1357-4310  
DOCUMENT TYPE: Literature Review  
RECORD TYPE: Citation  
LANGUAGE: English  
1997

26/3,AB/5 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2002 BIOSIS. All rts. reserv.

10198978 BIOSIS NO.: 199698653896  
**Immunization with a soluble recombinant HIV protein entrapped in biodegradable microparticles induces HIV-specific CD8+ cytotoxic T lymphocytes and CD4+ Th1 cells.**  
AUTHOR: Moore Anne; McGuirk Peter; Adams Susan; Jones Wendy C; McGee J Paul ; O'Hagan Derek T ; Mills Kingston H G(a  
AUTHOR ADDRESS: (a)Infection Immunity Lab., Biol. Dep., St. Patricks College, Maynooth, Co. Kildare\*\*Ireland  
JOURNAL: Vaccine 13 (18):p1741-1749 1995  
ISSN: 0264-410X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** One of the major obstacles to the development of successful recombinant vaccines against human immunodeficiency virus (HIV) and other intracellular pathogens is the identification of a safe and effective vaccine delivery system for the induction of cell mediated immunity with soluble protein antigens. In this study it was demonstrated that immunization with a recombinant HIV envelope (env) protein entrapped in biodegradable poly ( lactide -co- glycolide ) (PLG) **microparticles** induced consistent HIV-specific CD4+ and CD8+ T-cell responses in mice. Major histocompatibility complex (MHC) class I-restricted cytotoxic T lymphocytes (CTL) responses were detected following a single systemic immunization with gp120 entrapped **microparticles** and when given by the intranasal (i.n.) route induced HIV-specific CD8+ CTL and secretory IgA. Furthermore immunization with gp120 entrapped in **microparticles** generated CD4+ T cells that secreted moderate to high levels of IFN-gamma. Therefore, PLG **microparticles** are a safe and effective means of delivering antigen to the appropriate processing site for the generation of class I-restricted CTL, and are also capable of inducing Th1 cells.

1995

26/3,AB/6 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2002 BIOSIS. All rts. reserv.

09866921 BIOSIS NO.: 199598321839

Cholera toxin B subunit (CTB) entrapped in microparticles shows comparable immunogenicity to CTB mixed with whole cholera toxin following oral immunization.

AUTHOR: O'Hagan Derek T (a); McGee J Paul; Lindblad Marianne; Holmgren Jan  
AUTHOR ADDRESS: (a)United Biomed. Inc., 25 Davids Dr., Hauppauge, NY 11788  
\*\*USA

JOURNAL: International Journal of Pharmaceutics (Amsterdam) 119 (2):p  
251-255 1995

ISSN: 0378-5173

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Cholera toxin B subunit (CTB) was entrapped in poly ( lactide -co- glycolide ) microparticles and the responses induced by microencapsulated CTB were comparable to those induced by oral immunization with CTB mixed with whole cholera toxin. In addition, the CTB was released from microparticles intact following in vitro incubation, as determined by the ability of the CTB to bind to its cellular receptor, GM1. Moreover, microencapsulated CTB induced serum antibodies against intact CTB and not against monomeric fragments.

1995

26/3,AB/8 (Item 5 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2002 BIOSIS. All rts. reserv.

09863070 BIOSIS NO.: 199598317988

Zero order release of protein from poly (D, L - lactide -co- glycolide ) microparticles prepared using a modified phase separation technique.

AUTHOR: McGee J Paul; Davis Stanley S(a); O'Hagan Derek T

AUTHOR ADDRESS: (a)Dep. Pharmaceutical Sciences, University Nottingham,  
Nottingham NG7 2RD\*\*UK

JOURNAL: Journal of Controlled Release 34 (2):p77-86 1995

ISSN: 0168-3659

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The paper describes the preparation of poly (D, L - lactide -co- glycolide ) and poly (D, L - lactide ) microparticles with an entrapped protein using an adaptation of an existing phase separation technique. The effects of variations in microparticle preparation parameters such as the volume and concentration of polymer solution, the effect of different polymers and solvents, and the effect of non-ionic surfactants on the size, quality and loading level of the microparticles has been investigated. In vitro release studies were undertaken on selected batches of microparticles . The studies showed a small initial release of entrapped protein over the first 12 h, with the subsequent release profile appearing to follow zero order kinetics for microparticles with low levels of entrapped protein.

1995

26/3,AB/10 (Item 7 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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08857187 BIOSIS NO.: 1993 6008688

The preparation and characterization of poly ( lactide -co- glycolide ) microparticles : II. The entrapment of a model protein using a (water-in-oil)-in-water emulsion solvent evaporation technique.

AUTHOR: Jeffery Hayley; Davis Stanley S; O'Hagan Derek T (a  
AUTHOR ADDRESS: (a) Dep. of Pharmaceutical Sci., Univ. Nottingham,  
Nottingham NG7 2RD, England\*\*UK

JOURNAL: Pharmaceutical Research (New York) 10 (3):p362-368 1993

ISSN: 0724-8741

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** Poly ( lactide -co- glycolide ) (PLG) **microparticles** with entrapped antigens have recently been investigated as controlled-release vaccines. This paper describes the preparation of PLG **microparticles** with an entrapped model antigen, ovalbumin (OVA), using a (water-in-oil)-in-water emulsion solvent evaporation technique. In a series of experiments, the effects of process parameters on particle size and OVA entrapment were investigated. It was found that smooth, spherical **microparticles** 1-2  $\mu\text{m}$  in diameter containing up to 10% (w/w) OVA could be produced using a small volume of external aqueous phase containing a high concentration of emulsion stabilizer and a 1:5 antigen:polymer ratio. PAGE analysis, isoelectric focusing, and Western blotting of OVA released from the **microparticles** in vitro confirmed that the molecular weight and antigenicity of the protein remained largely unaltered by the entrapment procedure.

1993

26/3, AB/15 (Item 1 from file: 654)

DIALOG(R) File 654:US PAT.FULL.

(c) FORMAT ONLY 2002 THE DIALOG CORP. All rts. reserv.

02621127

Utility

PREPARATION OF **MICROPARTICLES** AND METHOD OF IMMUNIZATION

[ Dispersing bioactive material in oil medium which is nonsolvent for pharmaceutically acceptable polymer, adding said polymer dissolved in second medium, mixing to form **microparticles** ]

PATENT NO.: 5,603,960

ISSUED: February 18, 1997 (19970218)

INVENTOR(s): O'Hagan , Derek T., 16 Middlesex Rd., Bootle, Merseyside L20 9BW, GB (United Kingdom)

McGee, John P., Tanjong Kilmarnack Rd., Kilmarnock, Strathclyde KA3 2RB, GB (United Kingdom).Scotland

Davis, Stanley S., 19 Cavendish Crescent North, Nottingham NG7 1BA, GB (United Kingdom)  
[Assignee Code(s): 68000]

EXTRA INFO: Assignment transaction [Reassigned], recorded August 19, 1997 (19970819)

APPL. NO.: 8-374,751

FILED: June 02, 1995 (19950602)

PRIORITY: 9310781, GB (United Kingdom), May 25, 1993 (19930525)

PCT: PCT-US94-05834 (WO 94US5834)

Section 371 Date: June 02, 1995 (19950602)

Section 102(e) Date: June 02, 1995 (19950602)

Filing Date: May 24, 1994 (19940524)

Publication Number: WO94-27718 (WO 9427718)

Publication Date: December 08, 1994 (19941208)

FULL TEXT: 705 lines

ABSTRACT

The present invention describes a method for producing **microparticles** useful in the formulation of pharmaceutical compositions. The present invention further describes a method of immunizing a mammal against diseases comprising administering to a mammal an effective amount of antigen containing **microparticles**. In particular, the present invention describes a method of potentiating an immune response in a mammal comprising administering an effective amount of a pharmaceutical composition to a mammal. The present invention further describes a vaccine comprising a pharmaceutical composition containing said **microparticles**. An antigen delivery system comprising **microparticles** containing entrapped antigens is further described by the present invention. A pharmaceutical composition comprising **microparticles** and a pharmaceutical carrier is also provided.

?

41/3,AB/2 (Item 1 from file: 34)  
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

05140547 Genuine Article#: VC790 Number of References: 116

Title: **NASAL DELIVERY OF VACCINES** (Abstract Available)

Author(s): ALMEIDA AJ; ALPAR HO

Corporate Source: UNIV LISBON, FAC FARM, UNIDADE CIENCIAS & TECNOL  
FARMACEUT, AV FORCAS ARMADAS/P-1600 LISBON//PORTUGAL/; UNIV LISBON, FAC  
FARM, UNIDADE CIENCIAS & TECNOL FARMACEUT/P-1600 LISBON//PORTUGAL/;  
ASTON UNIV, INST PHARMACEUT SCI/BIRMINGHAM B4 7ET/W MIDLANDS/ENGLAND/

Journal: JOURNAL OF DRUG TARGETING, 1996, V3, N6, P455-467

ISSN: 1061-186X

Language: ENGLISH Document Type: REVIEW

Abstract: Only relatively recently the significance of inducing not only systemic immunity but also significant local immunity at susceptible mucosal surfaces has become appreciated. A new field of mucosal immunity has been established as information accumulates on mucosal-associated lymphoid tissue (MALT) and on its role in both local and systemic immune responses. This review describes the formulation of vaccines to be delivered to one of MALT components, i.e. the nasal-associated lymphoid tissue (NALT), which bears some similarities with the Peyer's patches of the intestine. The association of antigens with **adjuvants** and particulate carriers such as **microparticles**, nanoparticles and liposomes is emphasised.

41/3,AB/3 (Item 1 from file: 348)

DIALOG(R) File 348:EUROPEAN PATENTS

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00653535

Methods for administering biological agents and microparticle compositions useful in these and other methods.

Verfahren zur Verabreichung biologischer Stoffe sowie Mikropartikeln zur Verwendung in diesen und weiteren Verfahren.

Procedes pour l'administration d'agents biologiques et microparticules utilisables dans ces procedes et autrui.

PATENT ASSIGNEE:

ELI LILLY AND COMPANY, (204942), Lilly Corporate Center, Indianapolis Indiana 46285, (US), (applicant designated states:  
AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;NL;PT;SE)

INVENTOR:

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Ferguson, Thomas Harry, 1810 East Main, Greenfield, Indiana 46140, (US)  
Heiman, Mark Louis, 5740 Susan Drive East, Indianapolis, Indiana 46250, (US)

Thompson, William Webster, 5521 Overbrook Circle, Indianapolis, Indiana 46226-1542, (US)

LEGAL REPRESENTATIVE:

Tapping, Kenneth George et al (52302), Lilly Industries Limited European Patent Operations Erl Wood Manor, Windlesham Surrey GU20 6PH, (GB)

PATENT (CC, No, Kind, Date): EP 628307 A2 941214 (Basic)

APPLICATION (CC, No, Date): EP 94303655 940523;

PRIORITY (CC, No, Date): US 68413 930527; US 168941 931216

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE

INTERNATIONAL PATENT CLASS: A61K-009/16;

ABSTRACT EP 628307 A2

A method for administering biological agents to eggs is disclosed which comprises providing the agents in a particulate carrier and injecting the carrier into the air cells of the eggs. The egg is preferably maintained in a vertical position with the air cell on top to facilitate migration of the particulate carrier between the inner and outer membranes which

define the air cell, to the lower end of the egg. The particulate carrier releases the biological agent to the surrounding fluid and blood vessels. In addition, the carrier is embodied in the bird upon hatching from the egg, and therefore is available to continue to release the biological agent to the bird posthatch.

Also disclosed is a composition of polyester **microparticles** containing bioactive polypeptide agents and methods for preparing the composition and administering bioactive agents. The composition comprises biocompatible, biodegradable **microparticles** having a polyester matrix and from about 5% to about 25% by weight of a biologically active, water-soluble polypeptide dispersed throughout the matrix, the polypeptide selected from the group consisting of growth hormone releasing factor, synthetic analogs of growth hormone releasing factor, and pharmacologically active fragments thereof. The method for preparing the composition includes dissolving polyester in an organic solvent; suspending a biologically active agent in the polyester solution; emulsifying the suspension into an aqueous medium in which the agent is insoluble and evaporating the solvent from the emulsion to produce **microparticles**. The method for administering a bioactive agent to an organism involves suspending the **microparticles** in a suitable liquid and injecting the organism.

ABSTRACT WORD COUNT: 257

LANGUAGE (Publication, Procedural, Application): English; English; English  
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF2	349
SPEC A	(English)	EPABF2	11357
Total word count - document A			11706
Total word count - document B			0
Total word count - documents A + B			11706

41/3, AB/4 (Item 2 from file: 348)

DIALOG(R) File 348: EUROPEAN PATENTS  
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00558023

ORAL DELIVERY SYSTEMS FOR MICROPARTICLES  
SYSTEME ZUR ORALEN FREISETZUNG VON MIKROPARTIKELN  
SYSTEMES DE LIBERATION ORALE DE MICROPARTICULES

PATENT ASSIGNEE:

BIOTECH AUSTRALIA PTY. LIMITED, (1387311), 28 Barcoo Street, East Roseville, NSW 2069, (AU), (applicant designated states:  
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)

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PATENT (CC, No, Kind, Date): EP 531497 A1 930317 (Basic)  
EP 531497 A1 931222  
EP 531497 B1 970813  
WO 9217167 921015

APPLICATION (CC, No, Date): EP 92908034 920402; WO 92AU141 920402

PRIORITY (CC, No, Date): AU 915385 910402

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL;  
SE

INTERNATIONAL PATENT CLASS: A61K-009/50; A61K-009/52; A61K-047/24;  
A61K-047/42; A61K-047/46; A61K-047/48;

NOTE:

No A-document published by EPO

LANGUAGE (Publication, Procedural, Application): English; English; English  
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9708W2	785
CLAIMS B	(German)	9708W2	802
CLAIMS B	(French)	9708W2	973
SPEC B	(English)	9708W2	8706
Total word count - document A			0
Total word count - document B			11266
Total word count - documents A + B			11266

**41/3,AB/13 (Item 9 from file: 349)**

DIALOG(R)File 349:PCT FULLTEXT

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00338219

**DIRECT ADMINISTRATION OF GENE DELIVERY VEHICLES AT MULTIPLE SITES  
ADMINISTRATION DIRECTE EN PLUSIEURS SITES DE VEHICULES DISTRIBUTEURS DE GENES**

Patent Applicant/Assignee:

CHIRON VIAGENE INC,

Inventor(s):

IRWIN Michael J,

WARNER John F,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9620731 A1 19960711

Application: WO 95US16471 19951215 (PCT/WO US9516471)

Priority Application: US 94366784 19941230

Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN KE LS MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 16955

**English Abstract**

Methods of stimulating an immune response, either humoral or cell-mediated, in a warm-blooded animal through the administration at multiple sites of one or more gene delivery vehicles is provided. Each of the gene delivery vehicles directs the expression of at least one substance in host cells modified with the vehicle, such that an immune response is generated. Within preferred embodiments, the expressed substance elicits a cell-mediated immune response, preferably an HLA Class I-restricted immune response.

**French Abstract**

Methodes de stimulation d'une reponse immunitaire humorale ou cellulaire chez un animal a sang chaud par administration en plusieurs sites d'un ou plusieurs vehicules distributeurs de genes. Chacun de ces vehicules dirige l'expression d'au moins une substance dans des cellules hotes modifiees avec le vehicule de maniere a provoquer une reponse immunitaire. Dans les variantes preferees, la substance exprimee emet une reponse immunitaire induite par la cellule et de preference une reponse immunitaire par HLA restreinte a la categorie I.

**41/3,AB/14 (Item 10 from file: 349)**

DIALOG(R)File 349:PCT FULLTEXT

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00338186

**SURFACE-MODIFIED NANOPARTICLES AND METHOD OF MAKING AND USING SAME  
NANOParticules A MODIFICATION DE SURFACE ET LEURS PROCEDES DE FABRICATION  
ET D'UTILISATION**

Patent Applicant/Assignee:

THE BOARD OF REGENTS acting for and on behalf of THE UNIVERSITY OF MICHIGAN,

LEVY Robert J,  
LABHASETWAR Vinod D,  
SONG Cunxian S,

Inventor(s):

LEVY Robert J,  
LABHASETWAR Vinod D,  
SONG Cunxian S,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9620698 A2 19960711

Application: WO 96US476 19960104 (PCT/WO US9600476)

Priority Application: US 95369541 19950105; US 95389893 19950216

Designated States: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB  
GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL  
PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AZ  
BY KZ RU TJ TM AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF  
CG CI CM GA GN ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 33623

English Abstract

Biodegradable controlled release nanoparticles as sustained release bioactive agent delivery vehicles include surface modifying agents to target binding of the nanoparticles to tissues or cells of living systems, to enhance nanoparticle sustained release properties, and to protect nanoparticle-incorporated bioactive agents. Unique methods of making small (10 nm to 15 nm, and preferably 20 nm to 35 nm) nanoparticles having a narrow size distribution which can be surface-modified after the nanoparticles are formed is described. Techniques for modifying the surface include a lyophilization technique to produce a physically adsorbed coating and epoxy-derivatization to functionalize the surface of the nanoparticles to covalently bind molecules of interest. The nanoparticles may also comprise hydroxy-terminated or epoxide-terminated and/or activated multiblock copolymers, having hydrophobic segments which may be polycaprolactone and hydrophilic segments. The nanoparticles are useful for local intravascular administration of smooth muscle inhibitors and antithrombogenic agents as part of interventional cardiac or vascular catheterization such as a balloon angioplasty procedure; direct application to tissues and/or cells for gene therapy, such as the delivery of osteotropic genes or gene segments into bone progenitor cells; or oral administration in an enteric capsule for delivery of protein/peptide based vaccines.

French Abstract

Ces nanoparticules biodegradables a libération lente, utilisées comme véhicules d'apport d'agents bioactifs à libération prolongée, comprennent des agents de modification de surface qui assurent la liaison ciblee des nanoparticules avec des tissus ou des cellules de systèmes vivants, améliorent les propriétés de libération prolongée des nanoparticules et protègent les agents bioactifs incorporés dans lesdites nanoparticules. L'invention concerne également des procédés uniques de fabrication de nanoparticules de faibles dimensions (de 10 nm à 50 nm, de préférence de 20 nm à 35 nm), et présentant une répartition granulométrique étroite, qui peuvent être modifiées en surface après leur formation. Les techniques visant à modifier la surface des nanoparticules comprennent une technique de lyophilisation permettant de produire un enrobage adsorbé physiquement et une dérivation avec époxy permettant de fonctionnaliser la surface des nanoparticules de sorte qu'elles puissent lier de façon covalente des molécules importantes. Ces nanoparticules peuvent également comprendre des copolymères multisequences à activation et/ou terminaison époxyde ou hydroxy, présentant des segments hydrophobes qui peuvent être des segments de polycaprolactone ou hydrophiles. Elles conviennent à l'administration locale intravasculaire d'inhibiteurs des muscles lisses et d'agents antithrombogènes dans le cadre d'une intervention de sondage vasculaire ou cardiaque, telle qu'une procédure d'angioplastie à ballonnet; à une application directe sur des tissus

et/ou des cellules dans cadre de la therapie genique, par exemple l'apport de genes ou de segments de genes osteotropes dans les cellules osseuses souches; ou a l'administration par voie orale, dans une capsule entero-soluble destinee a l'apport de vaccins a base de proteines/peptides.

41/3,AB/15 (Item 11 from file: 349)  
DIALOG(R)File 349:PCT FULLTEXT  
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00337500

**METHODS FOR PREPARING AND PURIFYING MACROMOLECULAR CONJUGATES**  
**PROCEDES DE PREPARATION ET DE PURIFICATION DE CONJUGUES MACROMOLECULAIRES**

Patent Applicant/Assignee:

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Inventor(s):

DI Jie,

WOISZWILLO James E,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9620012 A2 19960704

Application: WO 95US16950 19951222 (PCT/WO US9516950)

Priority Application: US 94372820 19941223; US 95538817 19951004

Designated States: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 15988

**English Abstract**

Methods for the preparation and purification of conjugates by reacting a molecule containing an aldehyde group with a molecule containing an amine group in the presence of a polymer for a sufficient amount of time to form conjugate particles. Conjugates are prepared rapidly and efficiently by oxidizing the aldehyde and combining the oxidized aldehyde with a protein and polymer solution to form Schiff base intermediate conjugate particles in the absence of reductive amination. Subsequent separation of the particles from the conjugation reaction mixture yields purified conjugates that have been separated from the free, unconjugated components. Most preferably, the polymer is a polymer mixture comprising polyvinylpyrrolidone and polyethylene glycol. An organic solvent, such as an alcohol may be added to the incubation mixture to facilitate particle formation. A conjugating agent may also be included in the reaction mixture. The particles may be washed for removal of additional undesired contaminants and solubilized with a base, yielding soluble conjugates. Conjugates prepared from one or more antigens are suitable for use as a vaccine when administered to humans or animals.

**French Abstract**

Procedes de preparation et de purification de conjugues par reaction d'une molecule contenant un groupe aldehyde avec une molecule contenant un groupe amine en presence d'un polymere pendant une duree suffisante pour obtenir des particules de conjugues. On prepare les conjugues rapidement et efficacement par oxydation de l'aldehyde et par combinaison de l'aldehyde oxyde avec une solution a base de proteines et de polymere, afin d'obtenir des particules de conjugues intermediaires de base de Schiff en l'absence d'une animation reductrice. La separation subsequence des particules du melange reactionnel de conjugaison permet d'obtenir des conjugues purifies qu'on a separe des constituants libres non conjugues. De preference, le polymere est un melange de polymeres comprenant polyvinylpyrrolidone et polyethylene glycol. On peut ajouter un solvant organique, tel qu'un alcool, au melange d'incubation, afin de faciliter la formation des particules. On peut egalement ajouter un agent de conjugaison au melange reactionnel. On peut laver les particules afin de supprimer les contaminants supplementaires indesirables et les solubiliser au moyen d'une base, ce qui produit des conjugues solubles. Les conjugues prepares a partir d'un ou plusieurs antigenes sont utiles en tant que vaccins quand on les administre a l'homme ou a l'animal.

41/3,AB/18 (Item 14 from file: 349)  
DIALOG(R)File 349:PCT FULLTEXT  
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00321470

SOLID DELIVERY SYSTEMS FOR CONTROLLED RELEASE OF MOLECULES INCORPORATED  
THEREIN AND METHODS OF MAKING SAME  
SYSTEMES D'ADMINISTRATION DE SUBSTANCES SOLIDES, POUR LA LIBERATION  
CONTROLEE DE MOLECULES INCORPOREES DANS CES SUBSTANCES ET PROCEDES DE  
FABRICATION DE CES SYSTEMES

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Patent and Priority Information (Country, Number, Date):

Patent: WO 9603978 A1 19960215  
Application: WO 95GB1861 19950804 (PCT/WO GB9501861)  
Priority Application: GB 9415810 19940804; US 94349029 19941202

Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU  
IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD  
SE SG SI SK TJ TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR  
GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 20654

English Abstract

The present invention encompasses solid dose delivery systems for administration of guest substances. Preferred delivery systems are suitable for delivery of bioactive materials to subcutaneous and intradermal, intramuscular, intravenous tissue, the delivery system being sized and shaped for penetrating the epidermis. The delivery systems comprise a vitreous vehicle loaded with the guest substance and capable of releasing the guest substance in situ at various controlled rates. The present invention further includes methods of making and using the solid dose delivery systems.

French Abstract

Cette invention se rapporte a des systemes d'apport de doses de substances solides, qui servent a l'administration de substances hotes incorporees dans ces doses. Les systemes d'administration preferes de cette invention se pretent a l'apport de matieres bioactives dans des tissus intraveineux, intramusculaires, sous-cutanes et intradermiques, la taille et la forme de ce systeme d'apport etant concues pour lui permettre de penetrer dans l'epiderme. Ces systemes d'apport comprennent un excipient vitreux charge de la substance hote et capable de liberer cette substance hote in situ a divers taux controles. Cette invention se rapporte en outre a des procedes pour fabriquer et utiliser ces systemes d'administration de doses de substances solides.

41/3,AB/19 (Item 15 from file: 349)

00316942

**POLYMER MICROPARTICLES FOR DRUG DELIVERY**  
**MICROPARTICULES DE POLYMERES DESTINEES A L'APPORT DES MEDICAMENTS**

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Patent and Priority Information (Country, Number, Date):

Patent: WO 9535097 A1 19951228  
Application: WO 95GB1426 19950619 (PCT/WO GB9501426)  
Priority Application: GB 9412273 19940618

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IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD  
SE SG SI SK TJ TM TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR  
GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 8833

English Abstract

The invention provides a **microparticle** comprising a mixture of a biodegradable polymer and a water soluble polymer, and an active agent. Preferred biodegradable polymers are **lactide** homopolymers or copolymers of **lactide** and **glycolide**. Preferred water soluble polymers are PEG (poly(ethylene glycol)) or PEG copolymers. The particles exhibit a linear release profile of active agent. The invention also provides an emulsion/solvent extraction method to make the **microparticles**. The continuous phase of the secondary emulsion contains an organic solvent which is miscible with the organic solvent in the primary emulsion.

French Abstract

Cette invention concerne une microparticule comprenant un mélange formé d'un polymère biodegradable et d'un polymère soluble dans l'eau, et un agent actif. Les polymères biodegradables préférés sont les homopolymères de lactide ou les copolymères de lactide et de glycolide. Les polymères solubles dans l'eau préférés sont les polymères de PEG (poly(éthylène glycol)) ou les copolymères de PEG. Ces particules présentent un profil de libération linéaire de l'agent actif. Cette invention concerne également un procédé d'extraction par solvant/emulsion pour former les microparticules. La phase continue de l'emulsion secondaire contient un solvant organique qui se mélange avec le solvant organique présent dans l'emulsion principale.

41/3,AB/20 (Item 16 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00306777

**POLYMERIC GENE DELIVERY SYSTEM**  
**SYSTEME DE LIBERATION DE GENES POLYMERES**

Patent Applicant/Assignee:

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BOEKELHEIDE Kim,

Patent and Priority Information (Country, Number, Date):  
Patent: WO 9524929 A2 19950921  
Application: WO 95US3307 19950315 (PCT/WO US9503307)  
Priority Application: US 94668 19940315  
Designated States: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE  
Publication Language: English  
Fulltext Word Count: 9650

#### English Abstract

A means for obtaining efficient introduction of exogenous genes into a patient, with long term expression of the gene, is disclosed. The gene, under control of an appropriate promoter for expression in a particular cell type, is encapsulated or dispersed with a biocompatible, preferably biodegradable polymeric matrix, where the gene is able to diffuse out of the matrix over an extended period of time, for example, a period of three to twelve months or longer. The matrix is preferably in the form of a **microparticle** such as a microsphere (where the gene is dispersed throughout a solid polymeric matrix) or microcapsule (gene is stored in the core of a polymeric shell), a film, an implant, or a coating on a device such as a stent. The size and composition of the polymeric device is selected to result in favorable release kinetics in tissue. The size is also selected according to the method of delivery which is to be used, typically injection or administration of a suspension by aerosol into the nasal and/or pulmonary areas. The matrix composition can be selected to not only have favorable degradation rates, but to be formed of a material which is bioadhesive, to further increase the effectiveness of transfer when administered to a mucosal surface.

#### French Abstract

L'invention concerne un moyen efficace d'assurer l'introduction de gènes exogènes dans un patient, avec une expression prolongée du gène. Le gène, sous le contrôle d'un promoteur approprié pour l'expression dans un type de cellule particulier, est encapsulé ou dispersé dans une matrice polymère biocompatible de préférence biodegradable de laquelle le gène peut être diffusé sur une période prolongée, par exemple, une période de trois à douze mois. La matrice se présente, de préférence, sous la forme d'une microparticule telle qu'une microbille (ou les gènes sont dispersés dans une matrice polymère solide) ou de microcapsule (le gène est stocké dans le noyau d'une coquille polymère), de film, d'implant ou de revêtement sur un dispositif tel qu'un drain. La taille et la composition du dispositif polymère sont sélectionnées de sorte qu'une cinétique de libération avantageuse soit obtenue dans le tissu. La taille est également choisie selon la méthode de libération à utiliser, généralement l'injection ou l'administration d'une suspension par un aerosol dans les régions nasales et/ou pulmonaires. On peut sélectionner la composition de la matrice non seulement afin d'obtenir des vitesses de dégradation rapides avantageuses, mais également afin de permettre la formation d'un matériau bioadhésif et d'augmenter encore l'efficacité du transfert lorsque ce dernier est appliqué sur une surface muqueuse.

41/3,AB/21 (Item 17 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00285208

**BIODEGRADABLE PARTICLES**  
**PARTICULES BIODEGRADABLES**

Patent Applicant/Assignee:

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Inventor(s):

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MINAMITAKE Yoshiharu,  
LANGER Robert S,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9503357 A1 19950202

Application: WO 94US8416 19940722 (PCT/WO US9408416)  
Priority Application: US 93370 19930723; US 94677 19940318  
Designated States: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE  
Publication Language: English  
Fulltext Word Count: 10890

#### English Abstract

Particles are provided that are not rapidly cleared from the blood stream by the macrophages of the reticuloendothelial system, and that can be modified to achieve variable release rates or to target specific cells or organs. The particles have a biodegradable solid core containing a biologically active material and poly(alkylene glycol) moieties on the surface. The terminal hydroxyl group of the poly(alkylene glycol) can be used to covalently attach onto the surface of the particles biologically active molecules, including antibodies targeted to specific cells or organs, or molecules affecting the charge, lipophilicity or hydrophilicity of the particle. The surface of the particle can also be modified by attaching biodegradable polymers of the same structure as those forming the core of the particles. The typical size of the particles is between 1 nm and 1000 nm, preferably between 1 nm and 100 nm, although microparticles can also be formed as described herein. The particles can include magnetic particles or radiopaque materials, such as air and other gases, for diagnostic imaging, biologically active molecules to be delivered to a site, or compounds for targeting the particles. The particles have a prolonged half-life in the blood compared to particles not containing poly(alkylene glycol) moieties on the surface.

#### French Abstract

L'invention porte sur des particules qui ne sont pas rapidement éliminées du flux sanguin par les macrophages du système reticuloendothelial, et qui peuvent être modifiées pour obtenir des taux de libération variables ou pour viser des cellules ou organes spécifiques. Les particules ont un noyau solide biodegradable contenant de la matière biologiquement active et des fractions de poly(alkylene glycol) sur sa surface. Le groupe hydroxyle terminal du poly(alkylene glycol) permet la liaison covalente des molécules biologiquement actives sur la surface des particules, mais aussi des anticorps ayant pour cible des cellules ou organes spécifiques, ou des molécules affectant la charge, la lipophilie ou l'hydrophilie de la particule. Il est aussi possible de modifier la surface de la particule en fixant des polymères biodegradables de la même structure que ceux qui constituent le cœur des particules. La taille type des particules est comprise entre 1 nm et 1000 nm, généralement entre 1 nm et 100 nm, encore que des microparticules peuvent aussi se constituer selon le processus décrit ci-dessus. Parmi les particules en question peuvent figurer des particules magnétiques ou des matières radiopaques telles que l'air et d'autres gaz, utilisables pour l'imagerie diagnostique, des molécules biologiquement actives à livrer sur un site, ou des composés ayant ces particules pour cible. Ces particules ont une demi-vie dans le sang prolongée par rapport aux particules ne comportant pas de fractions poly(alkylene glycol) en surface.

41/3, AB/28 (Item 24 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00219932

ORAL DELIVERY SYSTEMS FOR MICROPARTICLES  
SYSTEMES DE LIBERATION ORALE DE MICROPARTICULES

Patent Applicant/Assignee:

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WESTWOOD Steven William,

Inventor(s):

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WESTWOOD Steven William,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9217167 A1 19921015

Application: WO 92AU141 19920402 (PCT/WO AU9200141)

Priority Application: AU 915385 19910402

Designated States: AT AU BE CA CH DE DK ES FR GB GR IT JP KR LU MC NL SE US

Publication Language: English

Fulltext Word Count: 11423

English Abstract

There are disclosed complexes and compositions for oral delivery of a substance or substances to the circulation or lymphatic drainage system of a host. The complexes of the invention comprise a **microparticle** coupled to at least one carrier, the carrier being capable of enabling the complex to be transported to the circulation or lymphatic drainage system via the mucosal epithelium of the host, and the **microparticle** entrapping or encapsulating, or being capable of entrapping or encapsulating, the substance(s). Examples of suitable carriers are mucosal binding proteins, bacterial adhesins, viral adhesins, toxin binding subunits, lectins, Vitamin B12 and analogues or derivatives of Vitamin B12 possessing binding activity to Castle's intrinsic factor.

French Abstract

On decrit des complexes et des compositions concus pour liberer par voie orale une ou plusieurs substance(s) dans le systeme de circulation ou de drainage lymphaatique d'un hote. Les complexes de l'invention comprennent une microparticule attachee a au moins un porteur, ledit porteur pouvant permettre le transport du compose dans le systeme de circulation ou de drainage lymphaatique via l'epithelium de la muqueuse de l'hote, et la microparticule piegeant ou encapsulant, ou pouvant pieger ou encapsuler, ladite ou lesdites substance(s). On peut citer comme exemple de porteurs appropries les proteines de liaison des muqueuses, les adhesines bacteriennes, les adhesines virales, les sous-unites de liaison des toxines, les lectines, la vitamine B12 et les analogues ou derives de la vitamine B12 dotes d'une activite de liaison au facteur de Castle.

41/3,AB/35 (Item 7 from file: 654)

DIALOG(R) File 654:US PAT.FULL.

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02593577

Utility

NANOPARTICLES AND **MICROPARTICLES** OF NON-LINEAR HYDROPHILIC-HYDROPHOBIC MULTIBLOCK COPOLYMERS

[Drug delivery]

PATENT NO.: 5,578,325

ISSUED: November 26, 1996 (19961126)

INVENTOR(s): Domb, Abraham J., Efrat, IL (Israel)

Gref, Ruxandra, Nancy, FR (France)

Minamitake, Yoshiharu, Ota, JP (Japan)

Peracchia, Maria T., Parma, IT (Italy)

Langer, Robert S., Newton, MA (Massachusetts), US (United States of America)

ASSIGNEE(s): Massachusetts Institute of Technology, (A U.S. Company or Corporation), Cambridge, MA (Massachusetts), US (United States of America)

[Assignee Code(s): 52912]

APPL. NO.: 8-265,440

FILED: June 24, 1994 (19940624)

The present application is a continuation-in-part of U.S. Ser. No. 08-210,677, "Biodegradable Injectable Particles for Imaging," filed Mar. 18, 1994, by Ruxandra Gref, Yoshiharu Minamitake and Robert S. Langer, which is a continuation-in-part of U.S. Ser. No. 08-096,370, "Biodegradable

**Microparticles** and **Injectable Nanoparticles**" filed Jun. 23, 1993, by Ruxandra Gref, Yoshiharu Minamitake and Robert S. Langer, the contents of which are hereby incorporated by reference.

This invention was made with government support under Grant Number NIH-1R01-GM44884 awarded by the National Institutes of Health. The government has certain rights in the invention.

FULL TEXT: 1133 lines

#### ABSTRACT

Injectable particles are provided that are not rapidly cleared from the blood stream by the macrophages of the reticuloendothelial system, and that can be modified as necessary to achieve variable release rates or to target specific cells or organs as desired. The injectable particles can include magnetic particles or radiopaque materials for diagnostic imaging, biologically active molecules to be delivered to a site, or compounds for targeting the particles. Biodistribution experiments indicate that the injectable particles have a prolonged half-life in the blood compared to particles not containing poly(alkylene glycol) moieties on the surface.

41/3,AB/39 (Item 11 from file: 654)

DIALOG(R) File 654:US PAT.FULL.

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02507722

Utility

METHOD FOR MAKING HYDROPHOBIC POLYMERIC **MICROPARTICLES**  
[Protein drug delivery]

PATENT NO.: 5,500,161

ISSUED: March 19, 1996 (19960319)

INVENTOR(s): Andrianov, Alexander K., Belmont, MA (Massachusetts), US  
(United States of America)  
Langer, Robert S., Newton, MA (Massachusetts), US (United  
States of America)

ASSIGNEE(s): Massachusetts Institute of Technology and Virus Research  
Institute, (A U.S. Company or Corporation), Cambridge, MA  
(Massachusetts), US (United States of America)  
[Assignee Code(s): 38169; 52912]

EXTRA INFO: Assignment transaction [Reassigned], recorded August 6,  
2001 (20010806)  
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Assignment transaction [Reassigned], recorded April 22,  
1996 (19960422)

APPL. NO.: 8-124,816

FILED: September 21, 1993 (19930921)

FULL TEXT: 657 lines

#### ABSTRACT

A method for the preparation of **microparticles**, and the product thereof, that includes dispersing a substantially water insoluble non-ionic or ionic polymer in an aqueous solution in which the substance to be delivered is also dissolved, dispersed or suspended, and then coagulating the polymer together with the substance by impact forces to form a **microparticle**. In an alternative embodiment, the **microparticle** is formed by coagulation of an aqueous polymeric dispersion through the use of electrolytes, pH changes, organic solvents in low concentrations (the minimal amount

necessary to break up the dispersion), or temperature changes to form polymer matrices encapsulating biological materials.  
?

59/3, AB/3 (Item 2 from File: 73)

DIALOG(R) File 73:EMBASE

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04915275 EMBASE No: 1992055490

**Native but not denatured recombinant human immunodeficiency virus type 1 gp120 generates broad-spectrum neutralizing antibodies in baboons**

Haigwood N.L.; Nara P.L.; Brooks E.; Van Nest G.A.; Ott G.; Higgins

K.W.; Dunlop N.; Scandella C.J.; Eichberg J.W.; Steimer K.S.

Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608-2916 United States

Journal of Virology (J. VIROL.) (United States) 1992, 66/1 (172-182)

CODEN: JOVIA ISSN: 0022-538X

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The protection of individuals from human immunodeficiency virus type 1 (**HIV -1**) infection with an envelope subunit derived from a single isolate will require the presentation of conserved epitopes in **gp120**. The objective of the studies presented here was to test whether a native recombinant **gp120** (rgp120) immunogen would elicit responses to conserved neutralization epitopes that are not present in a denatured recombinant **gp120** antigen from the same virus isolate. In a large study of 51 baboons, we have generated heterologous neutralizing activity with native, glycosylated rgp120(SF2) but not with denatured, nonglycosylated env 2-3(SF2). After repeated exposure to rgp120(SF2) formulated with one of several adjuvants, virus isolates from the United States, the Caribbean, and Africa were neutralized. The timing of the immunization regimen and the choice of adjuvant affected the virus neutralization titers both quantitatively and qualitatively. These results suggest that vaccination with native, glycosylated rgp120 from a single virus isolate, **HIV -SF2**, may elicit a protective immune response effective against geographically and sequentially distinct **HIV -1** isolates.

?

61/3,AB/1 / (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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11005259 BIOSIS NO.: 199799626404

**Antiretroviral DNA vaccine controlled release system from Poly (D, L - lactide -co- glycolide ) microparticles against HIV -1.**

AUTHOR: Hsu Yung-Yueh(a); Rasmussen Robert A; Trantolo Debra J(a); Gresser Joseph D(a); Wise Donald L

AUTHOR ADDRESS: (a)Cambridge Sci. Inc., Cambridge, MA\*\*USA

JOURNAL: Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 14 (4):pA30 1997

CONFERENCE/MEETING: National AIDS Malignancy Conference Bethesda, Maryland, USA April 28-30, 1997

ISSN: 1077-9450

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LANGUAGE: English

1997

61/3,AB/2 (Item 1 from file: 266)

DIALOG(R)File 266:FEDRIP

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00294769

IDENTIFYING NO.: 5R21AI48370-02 AGENCY CODE: CRISP

**MUCOSAL IMMUNITY TO HIV ENV BY ORAL VACCINATION**

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SPONSORING ORG.: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

FY : 2001

SUMMARY: DESCRIPTION: (Adapted from Applicant's Abstract) Accumulating evidence suggests that a combined regimen of immunization, in which a non-viral vector such as a DNA vaccine is given, followed by a viral vector such as vaccinia virus, results in robust CTL and CD4 T cell responses in mice and non-human primates. An important area of induction of cellular immunity to HIV that has not been much studied is the ability to induce CTL and humoral responses at mucosal surfaces. Yet, since most exposure to HIV occurs via mucosal surfaces, a successful prophylactic vaccine against HIV is likely to require a mucosal component. In these studies, we are seeking to define prime/boost strategies for the induction of high levels of mucosal immunity to HIV envelope (env) glycoprotein. We propose to explore the possibility of using poly (DL-lactide -co-glycolide ) (PLG) microparticles as vehicles for oral vaccination with plasmid DNA encoding gp160 in combination with recombinant viral vectors expressing the env gene products to enhance the antigen-specific mucosal and systemic immunity. The recombinant viruses used in these studies will include a replication-attenuated modified vaccinia virus Ankara (MVA), adeno-associated virus (AAV), and the E1/E3-deleted adenoviral (Ad) vector. The live vectors will be associated with liposomes for protection against gastric environment, increased transduction and vector dissemination in vivo. The overall goal of this effort is to derive ways to maximize the immunogenicity and safety of the HIV vaccine by inducing long-lasting protective immunity to the HIV env in mucosal and systemic sites. Furthermore, because systemic immunization with DNA plasmid or vaccinia virus does not induce antigen-specific immunity in mucosal tissues, the inductive sites of the mucosal immune system may still be naive to the live vectors delivered by oral vaccination. We hypothesize that oral vaccination with PLG-encapsulated DNA plasmid and liposome-associated non-replicating viral vectors expressing gp160 will augment the magnitude of immune responses to HIV env in mucosal and systemic tissues, and help to overcome the problem of preexisting immunity to the live vectors. The following specific aims will be pursued: i) to evaluate levels of

env-specific cellular and humoral responses in systemic and mucosal tissues (Peyer's patches and lamina propria) of gastrointestinal track after oral vaccination with a) PLG-encapsulated DNA plasmid encoding gp160, b) liposome-associated recombinant viral vectors expressing gp160, and c) a combination of PLG-encapsulated DNA plasmid and liposome-associated viral vectors expressing the env glycoprotein; ii) to determine whether oral vaccination overcomes the barrier to recombinant vaccinia or adenovirus immunization caused by preexisting immunity to these pathogens, and whether multiple oral immunizations with liposome-associated AAV-env enhance gp160-specific immunity; and iii) to analyze levels of protection in mucosal tissues induced by the oral vaccination against intrarectal challenge with recombinant vaccinia virus expressing gp160.

61/3,AB/3 (Item 1 from file: 348)

DIALOG(R) File 348:EUROPEAN PATENTS

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00448819

ENCAPSULATION PROCESS

EINKAPSELUNGSVERFAHREN

PROCEDE D'ENCAPSULATION

PATENT ASSIGNEE:

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PATENT (CC, No, Kind, Date): EP 471036 A1 920219 (Basic)  
EP 471036 A1 920318  
EP 471036 B1 960117  
WO 9013361 901115

APPLICATION (CC, No, Date): EP 90908830 900502; WO 90US2439 900502

PRIORITY (CC, No, Date): US 347476 890504

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: B01J-013/12; A61K-009/58; A61K-009/52;

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LANGUAGE (Publication,Procedural,Application): English; English; English

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CLAIMS B	(English)	EPAB96	1294
CLAIMS B	(German)	EPAB96	1248
CLAIMS B	(French)	EPAB96	1404
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Total word count - document A			0
Total word count - document B			9324
Total word count - documents A + B			9324

61/3,AB/4 (Item 1 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00408640

METHODS AND COMPOSITIONS FOR ENHANCING THE BIOADHESIVE PROPERTIES OF POLYMERS USING ORGANIC EXCIPIENTS

PROCEDES ET COMPOSITIONS UTILISANT DES EXCIPIENTS ORGANIQUES POUR RENFORCER LES PROPRIETES BIOADHESIVES DE POLYMERES

Patent Applicant/Assignee:

BROWN UNIVERSITY RESEARCH FOUNDATION,

Inventor(s):

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Patent and Priority Information (Country, Number, Date):

Patent: WO 9749385 A1 19971231  
Application: WO 97US10256 19970612 (PCT/WO US9710256)  
Priority Application: US 96326 19960625

Designated States: JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 13937

English Abstract

Methods and compositions are provided for enhancing the bioadhesive properties of polymers used in drug delivery systems. The bioadhesive properties of a polymer are enhanced by incorporating an anhydride oligomer into the polymer to enhance the ability of the polymer to adhere to a tissue surface such as a mucosal membrane. Anhydride oligomers which enhance the bioadhesive properties of a polymer include oligomers synthesized from dicarboxylic acid monomers, preferably those found in Krebs glycolysis cycle, especially fumaric acid. The oligomers can be incorporated within a wide range of polymers including proteins, polysaccharides and synthetic biocompatible polymers. In one embodiment, anhydride oligomers can be incorporated within polymers used to form or coat drug delivery systems, such as microspheres, which contain a drug or diagnostic agent. The oligomers can either be solubilized and blended with the polymer before manufacture or else used as a coating with polymers over existing systems. The polymers, for example in the form of microspheres, have improved ability to adhere to mucosal membranes, and thus can be used to deliver a drug or diagnostic agent via any of a range of mucosal membrane surfaces including those of the gastrointestinal, respiratory, excretory and reproductive tracts.

French Abstract

La presente invention concerne des procedes et compositions permettant de renforcer les proprietes bioadhesives de polymeres utilises dans les systemes d'administration de medicaments. En incorporant un oligomere d'anhydride dans le polymere on renforce ses proprietes bioadhesives ce qui fait que ce polymere adhère plus facilement à la surface d'un tissu tel qu'une membrane de muqueuse. Parmi les oligomeres d'anhydrides qui renforcent les proprietes bioadhesives d'un polymere, on trouve des oligomeres synthetises a partir de monomeres d'acide dicarboxylique, de preference les monomeres que l'on trouve dans le cycle de glycolyse de Krebs, et notamment l'acide fumarique. Ces oligomeres peuvent s'incorporer dans une large gamme de polymeres, y compris des proteines, des polyosides et des polymeres biocompatibles synthetiques. Selon une realisation, les oligomeres d'anhydrides peuvent s'incorporer dans des polymeres utilises pour former ou enrober les systemes d'administration de medicaments, tels que les microspheres, qui contiennent un medicament ou un agent de diagnostic. De tels polymeres, par exemple ceux qui se trouvent sous forme de microspheres, sont plus aptes à adherer aux membranes des muqueuses. Ils conviennent donc à l'administration d'un medicament ou d'un agent de diagnostic via diverses surfaces de membranes de muqueuses, et notamment celles des voies gastro-intestinales, respiratoires, excretrices et genitales.

61/3,AB/9 (Item 6 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00376320

MICROENCAPSULATED DNA FOR VACCINATION AND GENE THERAPY

ADN MICROENCAPSULE S'APPLIQUANT DANS DES PROCEDES DE VACCINATION ET DE THERAPIE GENIQUE

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Patent and Priority Information (Country, Number, Date):

Patent: WO 9717063 A1 19970515  
Application: WO 96GB2770 19961111 (PCT/WO GB9602770)  
Priority Application: GB 9523019 19951109; GB 961929 19960131

Designated States: AU CA JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL  
PT SE

Publication Language: English

Fulltext Word Count: 8386

English Abstract

A **microparticle** contains DNA coding for a polypeptide and oral administration of the **microparticle** leads to its expression. DNA coding for an immunogen is for stimulating antibody formation in a recipient and DNA coding for a non-immunogenic polypeptide is for gene therapy applications. DNA is incorporated into the **microparticle** without destruction of its function.

French Abstract

L'invention se rapporte à une microparticule contenant de l'ADN codant pour un polypeptide et l'administration par voie orale de cette microparticule qui conduit à son expression. L'ADN codant pour un immunogène est destiné à stimuler la formation d'anticorps chez un receveur, et l'ADN codant pour un polypeptide non-immunogène est destiné à être appliquée en thérapie génique. L'ADN est introduit dans la microparticule sans destruction de sa fonction.

61/3,AB/14 (Item 11 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00338219

**DIRECT ADMINISTRATION OF GENE DELIVERY VEHICLES AT MULTIPLE SITES**  
**ADMINISTRATION DIRECTE EN PLUSIEURS SITES DE VEHICULES DISTRIBUTEURS DE GENES**

Patent Applicant/Assignee:

CHIRON VIAGENE INC,

Inventor(s):

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Patent and Priority Information (Country, Number, Date):

Patent: WO 9620731 A1 19960711  
Application: WO 95US16471 19951215 (PCT/WO US9516471)  
Priority Application: US 94366784 19941230

Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN KE LS MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 16955

English Abstract

Methods of stimulating an immune response, either humoral or cell-mediated, in a warm-blooded animal through the administration at multiple sites of one or more gene delivery vehicles is provided. Each of the gene delivery vehicles directs the expression of at least one substance in host cells modified with the vehicle, such that an immune

response is generated. Within preferred embodiments, the expressed substance elicits a cell-mediated immune response, preferably an HLA Class I-restricted immune response.

#### French Abstract

Methodes de stimulation d'une reponse immunitaire humorale ou cellulaire chez un animal a sang chaud par administration en plusieurs sites d'un ou plusieurs vehicules distributeurs de genes. Chacun de ces vehicules dirige l'expression d'au moins une substance dans des cellules hotes modifiees avec le vehicule de maniere a provoquer une reponse immunitaire. Dans les variantes preferees, la substance exprimee emet une reponse immunitaire induite par la cellule et de preference une reponse immunitaire par HLA restreinte a la categorie I.

61/3,AB/16 (Item 13 from file: 349)  
DIALOG(R)File 349:PCT FULLTEXT  
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00306777

#### POLYMERIC GENE DELIVERY SYSTEM SYSTEME DE LIBERATION DE GENES POLYMERES

Patent Applicant/Assignee:

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Patent and Priority Information (Country, Number, Date):

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Priority Application: US 94668 19940315

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Publication Language: English

Fulltext Word Count: 9650

#### English Abstract

A means for obtaining efficient introduction of exogenous genes into a patient, with long term expression of the gene, is disclosed. The gene, under control of an appropriate promoter for expression in a particular cell type, is encapsulated or dispersed with a biocompatible, preferably biodegradable polymeric matrix, where the gene is able to diffuse out of the matrix over an extended period of time, for example, a period of three to twelve months or longer. The matrix is preferably in the form of a **microparticle** such as a microsphere (where the gene is dispersed throughout a solid polymeric matrix) or microcapsule (gene is stored in the core of a polymeric shell), a film, an implant, or a coating on a device such as a stent. The size and composition of the polymeric device is selected to result in favorable release kinetics in tissue. The size is also selected according to the method of delivery which is to be used, typically injection or administration of a suspension by aerosol into the nasal and/or pulmonary areas. The matrix composition can be selected to not only have favorable degradation rates, but to be formed of a material which is bioadhesive, to further increase the effectiveness of transfer when administered to a mucosal surface.

#### French Abstract

L'invention concerne un moyen efficace d'assurer l'introduction de genes exogenes dans un patient, avec une expression prolongee du gene. Le gene, sous le controle d'un promoteur approprie pour l'expression dans un type de cellule particulier, est encapsule ou disperse dans une matrice polymere biocompatibloe de preference biodegradable de laquelle le gene peut etre diffuse sur une periode prolongee, par exemple, une periode de trois a douze mois. La matrice se presente, de preference, sous la forme d'une microparticule telle qu'une microbille (ou les genes sont disperses dans une matrice polymere solide) ou de microcapsule (le gene est stocke

dans le noyau d'une coquille polymere), de film, d'implant ou de revetement sur un dispositif tel qu'un drain. La taille et la composition du dispositif polymere sont selectionnees de sorte qu'une cinetique de liberation avantageuse soit obtenue dans le tissu. La taille est egalement choisie selon la methode de liberation a utiliser, generalement l'injection ou l'administration d'une suspension par un aerosol dans les regions nasales et/ou pulmonaires. On peut selectionner la composition de la matrice non seulement afin d'obtenir des vitesses de degradacion rapides avantageuses, mais egalement afin de permettre la formation d'un materiau bioadhesif et d'augmenter encore l'efficacite du transfert lorsque ce dernier est applique sur une surface muqueuse.

61/3,AB/17 (Item 14 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00285208

**BIODEGRADABLE PARTICLES**  
**PARTICULES BIODEGRADABLES**

Patent Applicant/Assignee:

MASSACHUSETTS INSTITUTE OF TECHNOLOGY,

Inventor(s):

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MINAMITAKE Yoshiharu,  
LANGER Robert S,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9503357 A1 19950202

Application: WO 94US8416 19940722 (PCT/WO US9408416)

Priority Application: US 93370 19930723; US 94677 19940318

Designated States: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 10890

**English Abstract**

Particles are provided that are not rapidly cleared from the blood stream by the macrophages of the reticuloendothelial system, and that can be modified to achieve variable release rates or to target specific cells or organs. The particles have a biodegradable solid core containing a biologically active material and poly(alkylene glycol) moieties on the surface. The terminal hydroxyl group of the poly(alkylene glycol) can be used to covalently attach onto the surface of the particles biologically active molecules, including antibodies targeted to specific cells or organs, or molecules affecting the charge, lipophilicity or hydrophilicity of the particle. The surface of the particle can also be modified by attaching biodegradable polymers of the same structure as those forming the core of the particles. The typical size of the particles is between 1 nm and 1000 nm, preferably between 1 nm and 100 nm, although **microparticles** can also be formed as described herein. The particles can include magnetic particles or radiopaque materials, such as air and other gases, for diagnostic imaging, biologically active molecules to be delivered to a site, or compounds for targeting the particles. The particles have a prolonged half-life in the blood compared to particles not containing poly(alkylene glycol) moieties on the surface.

**French Abstract**

L'invention porte sur des particules qui ne sont pas rapidement eliminees du flux sanguin par les macrophages du systeme reticuloendothelial, et qui peuvent etre modifiees pour obtenir des taux de liberation variables ou pour viser des cellules ou organes specifiques. Les particules ont un noyau solide biodegradable contenant de la matiere biologiquement active et des fractions de poly(alkylene glycol) sur sa surface. Le groupe hydroxyle terminal du poly(alkylene glycol) permet la liaison covalente des molecules biologiquement actives sur la surface des particules, mais aussi des anticorps ayant pour cible

des cellules ou organes spécifiques, ou des molécules affectant la charge, la lipophilie ou l'hydrophilie de la particule. Il est aussi possible de modifier la surface de la particule en fixant des polymères biodegradables de la même structure que ceux qui constituent le cœur des particules. La taille type des particules est comprise entre 1 nm et 1000 nm, généralement entre 1 nm et 100 nm, encore que des microparticules peuvent aussi se constituer selon le processus décrit ci-dessus. Parmi les particules en question peuvent figurer des particules magnétiques ou des matières radiopaques telles que l'air et d'autres gaz, utilisables pour l'imagerie diagnostique, des molécules biologiquement actives à livrer sur un site, ou des composés ayant ces particules pour cible. Ces particules ont une demi-vie dans le sang prolongée par rapport aux particules ne comportant pas de fractions poly(alkylene glycol) en surface.

61/3,AB/29 (Item 8 from file: 654)  
DIALOG(R) File 654:US PAT.FULL.  
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02404782

Utility

MICROENCAPSULATION PROCESS AND PRODUCTS THEREFROM  
[Emulsification, solvent extraction]

PATENT NO.: 5,407,609

ISSUED: April 18, 1995 (19950418)

INVENTOR(s): Tice, Thomas R., Birmingham, AL (Alabama), US (United States of America)  
Gilley, Richard M., Birmingham, AL (Alabama), US (United States of America)

ASSIGNEE(s): Southern Research Institute, (A U.S. Company or Corporation),  
Birmingham, AL (Alabama), US (United States of America)  
[Assignee Code(s): 78536]

APPL. NO.: 8-62,696

FILED: May 17, 1993 (19930517)

This application is a continuation of application Ser. No. 07-347,476, filed May 4, 1989, now abandoned.

FULL TEXT: 870 lines

#### ABSTRACT

A method of microencapsulating an agent to form a microencapsulated product, having the steps of dispersing an effective amount of the agent in a solvent containing a dissolved wall forming material to form a dispersion, combining the dispersion with an effective amount of a continuous process medium to form an emulsion that contains the process medium and microdroplets having the agent, the solvent and the wall forming material and adding rapidly the emulsion to an effective amount of an extraction medium to extract the solvent from the microdroplets to form the microencapsulated product.

?

Detailed Description  
Claims  
Fulltext Word Count: 8845  
Publication Year: 1994

68/6/10 (Item 1 from file: 654)  
02588776

GELS FOR ENCAPSULATION OF BIOLOGICAL MATERIALS  
[Photopolymerization of acrylated resin, initiator]  
FULL TEXT: 2046 lines

68/6/11 (Item 2 from file: 654)  
02586181

MICROPARTICLE DELIVERY SYSTEM WITH A FUNCTIONALIZED SILICONE BONDED TO THE MATRIX  
FULL TEXT: 878 lines

68/6/12 (Item 3 from file: 654)  
02567679

METHOD AND KIT FOR MAKING A POLYSACCHARIDE-PROTEIN CONJUGATE  
[Vaccines]  
FULL TEXT: 461 lines

68/6/13 (Item 4 from file: 654)  
02552614

VISCOUS SUSPENSIONS OF CONTROLLED-RELEASE DRUG PARTICLES  
FULL TEXT: 643 lines

68/6/14 (Item 5 from file: 654)  
02540410

HYDROGEL MICROENCAPSULATED VACCINES  
[Mucosally administering a polyphosphazene polymer and antigen]  
FULL TEXT: 1385 lines  
?t s68/3,ab/1,2,3,5,8  
>>>No matching display code(s) found in file(s): 65, 123, 342, 345, 447,  
670

68/3,AB/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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09445198 BIOSIS NO.: 199497453568

The immunogenicity of a model protein entrapped in  
poly(lactide-co-glycolide) microparticles prepared by a novel phase  
separation technique.

AUTHOR: McGee J P; Davis S S; O'Hagan D T(a)

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UK

JOURNAL: Journal of Controlled Release 31 (1):p55-60 1994

ISSN: 0168-3659

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: A novel phase separation technique was used to prepare poly  
(lactide-co-glycolide) microparticles with an entrapped model protein,  
ovalbumin (OVA). In an in vitro release study, the entrapped OVA showed  
controlled release from the microparticles over about 10 to 15 days.  
Following subcutaneous (s.c.) immunization in mice, the microparticles  
induced a serum IgG antibody response that was significantly enhanced in  
comparison to the response induced by soluble OVA and was comparable to

the response induced by OVA adsorbed to an aluminium hydroxide adjuvant. The microparticles were also immunogenic by the oral route in mice and induced a serum IgG antibody response that was half the maximal response induced by s.c. immunization with OVA adsorbed to the adjuvant.

1994

68/3,AB/2 (Item 1 from file: 34)  
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

01878848 Genuine Article#: JH930 Number of References: 33  
**Title: BIODEGRADABLE POLY(DL-LACTIDE-CO-GLYCOLIDE) MICROSPHERES**  
Author(s): ELDRIDGE JH; STAAS JK; TICE TR; GILLEY RM  
Corporate Source: UNIV ALABAMA,DEPT MED,UNIV STN/BIRMINGHAM//AL/35294; SO  
RES INST,DIV CONTROLLED RELEASE/BIRMINGHAM//AL/35205; UNIV ALABAMA,DEPT  
MICROBIOL/BIRMINGHAM//AL/35294  
Journal: RESEARCH IN IMMUNOLOGY, 1992, V143, N5 (JUN), P557-563  
Language: ENGLISH Document Type: ARTICLE

68/3,AB/3 (Item 1 from file: 349)  
DIALOG(R) File 349:PCT FULLTEXT  
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00337500

**METHODS FOR PREPARING AND PURIFYING MACROMOLECULAR CONJUGATES**  
**PROCEDES DE PREPARATION ET DE PURIFICATION DE CONJUGUES MACROMOLECULAIRES**

Patent Applicant/Assignee:

MIDDLESEX SCIENCES INC,

Inventor(s):

DI Jie,

WOISZWILLO James E,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9620012 A2 19960704

Application: WO 95US16950 19951222 (PCT/WO US9516950)

Priority Application: US 94372820 19941223; US 95538817 19951004

Designated States: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 15988

#### English Abstract

Methods for the preparation and purification of conjugates by reacting a molecule containing an aldehyde group with a molecule containing an amine group in the presence of a polymer for a sufficient amount of time to form conjugate particles. Conjugates are prepared rapidly and efficiently by oxidizing the aldehyde and combining the oxidized aldehyde with a protein and polymer solution to form Schiff base intermediate conjugate particles in the absence of reductive amination. Subsequent separation of the particles from the conjugation reaction mixture yields purified conjugates that have been separated from the free, unconjugated components. Most preferably, the polymer is a polymer mixture comprising polyvinylpyrrolidone and polyethylene glycol. An organic solvent, such as an alcohol may be added to the incubation mixture to facilitate particle formation. A conjugating agent may also be included in the reaction mixture. The particles may be washed for removal of additional undesired contaminants and solubilized with a base, yielding soluble conjugates. Conjugates prepared from one or more antigens are suitable for use as a vaccine when administered to humans or animals.

#### French Abstract

Procedes de preparation et de purification de conjugues par reaction d'une molecule contenant un groupe aldehyde avec une molecule contenant un groupe amine en presence d'un polymere pendant une duree suffisante pour obtenir des particules de conjugues. On prepare les conjugues

rapidement et efficacement par oxydation de l'aldehyde et par combinaison de l'aldehyde oxyde avec une solution à base de protéines et de polymère, afin d'obtenir des particules de conjugues intermédiaires de base de Schiff en l'absence d'une animation réductrice. La séparation subséquente des particules du mélange réactionnel de conjugaison permet d'obtenir des conjugues purifiés qu'on a séparé des constituants libres non conjugues. De préférence, le polymère est un mélange de polymères comprenant polyvinylpyrrolidone et polyéthylene glycol. On peut ajouter un solvant organique, tel qu'un alcool, au mélange d'incubation, afin de faciliter la formation des particules. On peut également ajouter un agent de conjugaison au mélange réactionnel. On peut laver les particules afin de supprimer les contaminants supplémentaires indésirables et les solubiliser au moyen d'une base, ce qui produit des conjugues solubles. Les conjugues préparés à partir d'un ou plusieurs antigènes sont utiles en tant que vaccins quand on les administre à l'homme ou à l'animal.

68/3,AB/5 (Item 3 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00313034

**MICROPARTICLE DELIVERY SYSTEM**

**SYSTEME DE LIBERATION DE MICROPARTICULES**

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Patent and Priority Information (Country, Number, Date):

Patent: WO 9531187 A1 19951123

Application: WO 95CA294 19950518 (PCT/WO CA9500294)

Priority Application: US 94245646 19940518

Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU  
JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE  
SI SK TJ TT UA US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT  
LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 9729

**English Abstract**

A particulate carrier for an agent comprising a solid core of a polysaccharide and a proteinaceous material and an organometallic polymer bonded to the core is provided. The agent has a biological activity, such as immunogenicity, and may comprise the proteinaceous material or be a separate component of the core. Polysaccharide cores include dextran, starch, cellulose and derivatives thereof and the organometallic polymer includes silicones including substituted silicones. The particulate carriers are useful for delivering agents to the immune system of a subject by mucosal or parenteral administration to produce immune responses, including antibody responses.

**French Abstract**

L'invention concerne un excipient particulaire destiné à un agent comprenant un noyau solide d'un polysaccharide et une matière protéique, ainsi qu'un polymère organométallique lié au noyau. Cet agent présente

une activite biologique, par exemple une immunogenicite, ce peut comprendre la matiere proteique ou etre un constituant separe du noyau. Les noyaux de polysaccharide comprennent le dextrane, l'amidon, la cellulose et ses derives. Le polymere organometallique comprend les silicones, y compris les silicones substituees. Ces excipients particulaires sont utiles pour la liberation d'agents vers le systeme immunitaire d'un sujet, par les muqueuses ou par voie parenterale, dans le but de provoquer des reponses immunitaires, y compris la production d'anticorps.

68/3,AB/8 (Item 6 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00267465

**INDUCING CYTOTOXIC T LYMPHOCYTE RESPONSES**

**PROCEDE PERMETTANT D'INDUIRE DES REONSES DE LYMPHOCYTES-T CYTOTOXIQUES**

Patent Applicant/Assignee:

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ROCK Kenneth,

Inventor(s):

ROCK Kenneth,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9415635 A1 19940721

Application: WO 94US362 19940110 (PCT/WO US9400362)

Priority Application: US 933233 19930111

Designated States: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT  
SE

Publication Language: English

Fulltext Word Count: 13292

**English Abstract**

The invention provides compositions and methods for inducing MHC class I-restricted cytotoxic T lymphocyte responses in a mammalian host by immunization with non-replicating protein antigens. The compositions of the invention comprise a particulate-protein complex capable of inducing a class I-restricted CTL response to a protein antigen in a mammal, in which the particulate protein complex comprises a particulate component having an average diameter ranging in size from about .5μm to about 6μm, linked to a non-replicating protein antigen derived from a tumor cell or from pathogenic organism where CTL response is likely to play an important role in conferring protective immunity in a mammal, with the proviso that the particulate component is not a prokaryotic or eukaryotic cell, or a micellar, multimicellar, or liposome vesicle composed of detergents or lipids. The non-replicating protein antigen is attached to the particle component through a covalent or non-covalent association to form particulate protein antigen complexes and the complexes are administered to a mammalian host in conjunction with a pharmaceutically acceptable excipient, in a CTL-stimulatory amount. The invention also provides non-replicating vaccines and methods of vaccinating a mammalian host against pathogenic diseases or tumors for CTL immunity.

**French Abstract**

L'invention se rapporte a des compositions et a des procedes permettant d'induire des reponses de lymphocytes-T cytotoxiques (CTL) restreints par le complexe majeur d'histocompatibilite (CMH) de classe I, par immunisation avec des antigenes proteiques sans replication. Les compositions de l'invention comprennent un complexe substance-particulaire-proteine capable d'induire une reponse de CTK CMH-classe I-restreint par rapport a un antigen proteique chez un mammifere, ledit complexe comprenant un constituant particulaire presentant un diametre moyen compris entre environ 0,5 μm et environ 6μm, lie a un antigen proteique sans replication derive d'une cellule tumorale ou d'un organisme pathogene, lorsque la reponse de CTL sera apte a contribuer de facon importante a l'apparition d'une immunite

protectrice chez un mammifère, et a condition que le constituant particulaire ne soit pas une cellule procaryotique ou eucaryotique, ou une vesicule micellaire, multimicellaire ou liposomique composee de detergents ou de lipides. L'antigène protéique sans replication est fixe au constituant particulaire par une association covalente ou noncovalente pour former des complexes substance particulière-antigène protéique, et les complexes sont administrés à un mammifère-hôte conjointement avec un excipient pharmaceutiquement acceptable, et en une dose stimulante par rapport aux CTL. L'invention se rapporte également à des vaccins sans replication et à des procédés de vaccination d'un mammifère-hôte contre des maladies pathogènes ou des tumeurs et afin de lui conferer une immunité par CTL.

?

73/3,AB/1 (Item 1 from file: 155)  
DIALOG(R) File 155: MEDLINE(R)

08423846 95169513 PMID: 7865332

**Accell particle-mediated DNA immunization elicits humoral, cytotoxic, and protective immune responses.**

Haynes JR; Fuller DH; Eisenbraun MD; Ford MJ; Pertmer TM

Agracetus, Inc., Middleton, Wisconsin 53562.

AIDS research and human retroviruses (UNITED STATES) 1994, 10 Suppl 2  
pS43-5, ISSN 0889-2229 Journal Code: ART

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Accell particle-mediated gene delivery technology was employed for the intracellular delivery of antigen-encoding expression vectors in epidermal tissues in laboratory animals. Delivery of plasmid **DNA**-coated gold **microparticles** using the Accell gene delivery system resulted in de novo antigen expression in epidermal cells that stimulated the induction of antigen-specific humoral and cytotoxic cellular immune responses. Optimal **DNA** delivery conditions favoring maximal humoral responses required the delivery of  $5 \times 10^7$  micron-sized gold particles containing 300 plasmid copies per particle (80 ng of vector total) into a 4-cm<sup>2</sup> area of abdominal skin. Comparison of immune responses between animals that received intramuscular injections of relatively large quantities of vector **DNA** (100 micrograms) and those that received intracellular deliveries of submicrogram quantities of the same **DNA** to the epidermis demonstrated that the latter approach was considerably more effective at eliciting strong humoral responses. In addition, cytotoxic cellular immune responses were elicited to **HIV -1 gp120** following epidermal delivery of **HIV -1 gp160** or **gp120** expression constructs. A qualitative shift from predominantly cytotoxic cellular to predominantly humoral immune responses with continued immunization indicated the potential for optimizing delivery conditions to favor specifically one type of response over the other.

73/3,AB/2 (Item 1 from file: 34)  
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci  
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03627079 Genuine Article#: PT118 Number of References: 8

**Title: ACCELL(R) PARTICLE-MEDIATED DNA IMMUNIZATION ELICITS HUMORAL, CYTOTOXIC, AND PROTECTIVE IMMUNE-RESPONSES** (Abstract Available)

Author(s): HAYNES JR; FULLER DH; EISENTRAUT MD; FORD MJ; PERTMER TM

Corporate Source: AGRACETUS INC, 8520 UNIV GREEN/MIDDLETON//WI/53562

Journal: AIDS RESEARCH AND HUMAN RETROVIRUSES, 1994, V10, S2, PS43-S45

ISSN: 0889-2229

Language: ENGLISH Document Type: ARTICLE

Abstract: Accell(R) particle-mediated gene delivery technology was employed for the intracellular delivery of antigen-encoding expression vectors in epidermal tissues in laboratory animals. Delivery of plasmid **DNA**-coated gold **microparticles** using the Accell gene delivery system resulted in de novo antigen expression in epidermal cells that stimulated the induction of antigen-specific humoral and cytotoxic cellular immune responses. Optimal **DNA** delivery conditions favoring maximal humoral responses required the delivery of  $5 \times 10^7$  micron-sized gold particles containing 300 plasmid copies per particle (80 ng of vector total) into a 4-cm<sup>2</sup> area of abdominal skin.

Comparison of immune responses between animals that received intramuscular injections of relatively large quantities of vector **DNA** (100  $\mu$ g) and those that received intracellular deliveries of submicrogram quantities of the same **DNA** to the epidermis demonstrated that the latter approach was considerably more effective at eliciting strong humoral responses. In addition, cytotoxic cellular immune responses were elicited to **HIV -1 gp120** following epidermal delivery of **HIV -1 gp160** or **gp120** expression constructs. A qualitative

shift from predominantly cytotoxic cellular to predominantly humoral immune responses with continued immunization indicated the potential for optimizing delivery conditions to favor specifically one type of response over the other.

73/3,AB/3 (Item 1 from file: 76)  
DIALOG(R)File 76:Life Sciences Collection  
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01891219 3699084

Accell registered particle-mediated DNA immunization elicits humoral, cytotoxic, and protective immune responses

Haynes, J.R.; Fuller, D.H.; Eisenbraun, M.D.; Ford, M.J.; Pertmer, T.M.

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AIDS RES. HUM. RETROVIRUSES vol. 10, no. 2 suppl., pp. S43-S45 (1994)

ISSN: 0889-2229

DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH

SUBFILE: Virology & AIDS Abstracts

Accell registered particle-mediated gene delivery technology was employed for the intracellular delivery of antigen-encoding expression vectors in epidermal tissues in laboratory animals. Delivery of plasmid DNA -coated gold **microparticles** using the Accell gene delivery system resulted in de novo antigen expression in epidermal cells that stimulated the induction of antigen-specific humoral and cytotoxic cellular immune responses. Optimal DNA delivery conditions favoring maximal humoral responses required the delivery of 5 x 10 super(7) micron-sized gold particles containing 300 plasmid copies per particle (80 ng of vector total) into a 4-cm super(2) area of abdominal skin. Comparison of immune responses between animals that received intramuscular injections of relatively large quantities of vector DNA (100 mu g) and those that received intracellular deliveries of submicrogram quantities of the same DNA to the epidermis demonstrated that the latter approach was considerably more effective at eliciting strong humoral responses. In addition, cytotoxic cellular immune responses were elicited to HIV -1 gp120 following epidermal delivery of HIV -1 gp160 or gp120 expression constructs. A qualitative shift from predominantly cytotoxic cellular to predominantly humoral immune responses with continued immunization indicated the potential for optimizing delivery conditions to favor specifically one type of response over the other.

73/3,AB/7 (Item 3 from file: 348)  
DIALOG(R)File 348:EUROPEAN PATENTS  
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00671556

Derivatives of gp160 and vaccines based on gp160 or a derivative thereof, containing an adjuvant.

GP160 Derivate und Adjuvans enthaltende Impfstoffe auf Basis von GP160 oder dessen Derivate.

Derives de gp160 et vaccines a base de gp160 ou d'un de ses derives, contenant un adjuvant.

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PATENT (CC, No, Kind, Date): EP 644201 A1 950322 (Basic)

APPLICATION (CC, No, Date): EP 94202409 910921;

PRIORITY (CC, No, Date): GB 9021175 900928; GB 9106048 910321

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

RELATED PARENT NUMBER(S) - PN (AN):

EP 550485 (EP 919160671)

INTERNATIONAL PATENT CLASS: C07K-014/16; C12N-015/49; A61K-039/39;

A61K-039/21;

ABSTRACT EP 644201 A1

This invention provides novel, substantially uncleavable forms of gp160, and vaccine formulations containing gp160 or a derivative thereof, adjuvanted with 3-D Mpl. The compositions are useful for the immunotherapeutic and immunoprophylactic treatment of HIV infections.

ABSTRACT WORD COUNT: 39

LANGUAGE (Publication, Procedural, Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	246
SPEC A	(English)	EPAB95	6954
Total word count - document A			7200
Total word count - document B			0
Total word count - documents A + B			7200

73/3, AB/42 (Item 25 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00219322

DERIVATIVES OPF GP160 AND VACCINES BASED ON GP160 OR A DERIVATIVE THEREOF, CONTAINING AN ADJUVANT  
DERIVES DE GP160 ET VACCINS A BASE DE GP160 OU D'UN DE SES DERIVES  
CONTENANT UN ADJUVANT

Patent Applicant/Assignee:

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Inventor(s):

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SLAOUI Moncef,  
BRUCK Claudine,  
FRANCOTTE Myriam,  
KUMMERT Suzy,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9216556 A1 19921001

Application: WO 91EP2047 19911025 (PCT/WO EP9102047)

Priority Application: GB 916048 19910321

Designated States: BR CS FI HU NO PL

Publication Language: English

Fulltext Word Count: 8913

English Abstract

This invention provides novel, substantially uncleavable forms of gp160, and vaccine formulations containing gp160 or a derivative thereof, adjuvanted with 3-D Mpl. The compositions are useful for the immunotherapeutic and immunoprophylactic treatment of HIV infections.

French Abstract

L'invention decrit de nouvelles formes de GP160, pratiquement indivisibles, ainsi que des formulations de vaccins contenant GP160 ou un de ses derives, auxquelles on a ajoute un adjuvant, notamment 3-D Mpl.

Les compositions sont efficaces pour le traitement immunothérapeutique et immunoprophylactique des infections par **HIV** .

?

00256409

PEPTIDE INHIBITORS OF INFLAMMATION MEDIATED BY SELECTINS  
INHIBITEURS PEPTIDIQUES D'INFLAMMATION PRÉSENTANT UNE MÉDIATION PAR LES  
SELECTINES

Patent Applicant/Assignee:

CENTOCOR INC,  
BOARD OF REGENTS OF THE UNIVERSITY OF OKLAHOMA,

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GENG Jian-Guo,  
RIEXINGER Douglas J,  
KRUSZYNSKI Marian,  
EPPS Leon A,  
MERVIC Miljenko,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9404568 A1 19940303  
Application: WO 92US10986 19921217 (PCT/WO US9210986)  
Priority Application: US 91942 19911218

Designated States: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 12413

English Abstract

Peptides derived from three regions of the lectin domain of GMP-140 (P-selectin) and the related selectins, ELAM-1 (E-selectin) and the lymphocyte homing receptor (L-selectin), have been found to inhibit neutrophil adhesion to GMP-140. These and additional peptides have been synthesized, having as their core region portions of the 74-76 amino acid sequence of GMP-140, with residue 1 defined as the N-terminus of the mature protein after the cleavage of the signal peptide. Examples demonstrate the inhibition of the binding of neutrophils to GMP-140 of peptides in concentrations ranging from 30 to 1500 mumol. It has been found that alterations within the core sequence, as well as N-terminal and C-terminal flanking regions, do not result in loss of biological activity. The peptides are useful as diagnostics and, in combination with a suitable pharmaceutical carrier, for clinical applications in the modulation or inhibition of coagulation processes or inflammatory processes.

French Abstract

On a decouvert que des peptides derives de trois regions du domaine lectine de GMP-140 (selectine P) et des selectines apparentees, ELAM-1 (selectine E) et le recepteur de guidage lymphocytaire (selectine L), inhibent l'adherence des neutrophiles a GMP-140. Ces peptides et d'autres ont ete synthetises et ils comportent en guise de region centrale des portions de la sequence d'acide amine 74-76 de GMP-140, le residu 1 etant defini comme le terminal N de la proteine mature apres coupure du peptide de signal. Des exemples demontront l'inhibition de la liaison de neutrophiles avec GMP-140 par des peptides a des concentrations allant de 30 a 1500 mumol. On a decouvert que des modifications survenant dans la sequence centrale, ainsi que dans des regions adjacentes des terminaux N et C, n'entraînent aucune diminution d'activite biologique. Ces peptides sont utiles pour le diagnostic et, combines avec un vecteur pharmaceutique approprie, pour des applications cliniques concernant la modulation ou l'inhibition des processus de coagulation ou d'inflammation.

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87/3,AB/2 (Item 1 from file: 349)  
DIALOG(R)File 349:PCT FULLTEXT  
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00266667

**PEPTIDE INHIBITORS OF SELECTIN BINDING**  
**INHIBITEURS PEPTIDIQUES DE LIAISON DE SELECTINE**

Patent Applicant/Assignee:

CENTOCOR INC,  
HEAVNER George A,  
KRUSZYNSKI Marian,

Inventor(s):

HEAVNER George A,  
KRUSZYNSKI Marian,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9414836 A1 19940707  
Application: WO 93US12110 19931213 (PCT/WO US9312110)  
Priority Application: US 92771 19921218

Designated States: CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 13607

**English Abstract**

The present invention provides novel peptides having as their core region portions of the 109-118 amino acid sequence of P-selectin, E-selectin or L-selectin. The invention also provides pharmaceutical compositions comprising the peptides of the invention, and diagnostic and therapeutic methods utilizing the peptides and pharmaceutical compositions of the invention.

**French Abstract**

La presente invention se rapporte à de nouveaux peptides comprenant au niveau de leur région centrale des parties de la séquence d'aminoacides 109-118 de P-selectine, E-selectine ou L-selectine. L'invention se rapporte également à des compositions pharmaceutiques comprenant les peptides de l'invention, ainsi qu'à des procédés diagnostiques et thérapeutiques consistant à utiliser les peptides et les compositions pharmaceutiques de l'invention.

87/3,AB/3 (Item 2 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT  
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00257150

**PEPTIDE INHIBITORS OF CELLULAR ADHESION**  
**INHIBITEURS PEPTIDIQUES D'ADHESION CELLULAIRE**

Patent Applicant/Assignee:

CENTOCOR INC,  
HEAVNER George A,

Inventor(s):

HEAVNER George A,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9405310 A1 19940317  
Application: WO 93US8504 19930908 (PCT/WO US9308504)  
Priority Application: US 92653 19920908

Designated States: CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 59995

**English Abstract**

Novel cyclic peptides of the selectin 54-63 sequence exhibit unexpected and desired properties. Specific points of cyclization or conformational restriction in conjunction with specific substitutions have been identified that not only unexpectedly enhance the biological activity of

these compounds, but also significantly increase their resistance to enzymatic degradation. Formulas of the active compounds and representative examples of preferred peptides are presented herein.

#### French Abstract

De nouveaux peptides cycliques de la sequence (54-63) de selectine presentent des proprietes inattendues et voulues. On a identifie des points specifiques de cyclisation ou de restriction de conformation conjointement avec des substitutions specifiques qui non seulement ameliorent de facon inattendue l'activite biologique de ces composes, mais egalement accroissent significativement leur resistance a la degradation enzymatique. L'invention concerne egalement des formules des composes actifs et des exemples representatifs de peptides preferes.

87/3,AB/4 (Item 3 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00250230

#### PEPTIDE INHIBITORS OF SELECTIN BINDING

#### PEPTIDES INHIBITEURS DE LA LIAISON DE SELECTINE

Patent Applicant/Assignee:

CENTOCOR INC,

Inventor(s):

HEAVNER George A,

RIEXINGER Douglas,

MERVIC Miljenko,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9324527 A1 19931209

Application: WO 93US3986 19930428 (PCT/WO US9303986)

Priority Application: US 92986 19920528

Designated States: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 11356

#### English Abstract

The present invention provides peptides comprising portions of the amino acid sequence at positions 58-61 of P-selectin. The invention also provides pharmaceutical compositions comprising the peptides of the invention, diagnostic and therapeutic methods utilizing the peptides and pharmaceutical compositions of the invention, and method of preparing the peptides and pharmaceutical compositions.

#### French Abstract

La presente invention se rapporte a des peptides comprenant des parties de la sequence d'acides amines aux positions 58-61 de la selectine P. L'invention se rapporte egalement a des compositions pharmaceutiques comprenant lesdits peptides, des procedes therapeutiques et de diagnostic utilisant les peptides et les compositions pharmaceutiques de l'invention, et un procede de preparation des peptides et des compositions pharmaceutiques.

87/3,AB/10 (Item 4 from file: 654)

DIALOG(R)File 654:US PAT.FULL.

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02170042

Utility

#### FUNCTIONALLY ACTIVE SELECTIN-DERIVED PEPTIDES

[Polypeptide antiinflammatory agents or anticoagulants]

PATENT NO.: 5,198,424

ISSUED: March 30, 1993 (19930330)

INVENTOR(s): McEver, Rodger P., Oklahoma City, OK (Oklahoma), US (United

States of America)  
ASSIGNEE(s): Board of Regents of the University of Oklahoma, (A U.S.  
Company or Corporation ), Norman, OK (Oklahoma), US (United  
States of America)  
[Assignee Code(s): 61802]  
APPL. NO.: 7-867,271  
FILED: April 07, 1992 (19920407)

This is a continuation of copending application Ser. No. 07-554,199 filed on Jul. 17, 1990 abandoned, which is a continuation-in-part of U.S. Ser. No. 07-320,408 entitled "Method for Modulation of Inflammatory Responses" filed Mar. 8, 1989 by Rodger P. McEver.

The U.S. Government has rights in this invention by virtues of grants from the National Heart, Lung and Blood Institute.

FULL TEXT: 1081 lines

#### ABSTRACT

Peptides derived from three regions of the lectin binding region of GMP-140 have been found to selectively interact with "selectins", including GMP-140, ELAM-1, and lymphocyte homing receptor. The peptides can be as short as eight to thirteen amino acids in length and are easily prepared and modified by standard techniques. Critical elements of the counter-receptor or ligand on the neutrophils which binds GMP-140 are also identified. The peptides are useful as diagnostics and

The U.S. Government has rights in this invention by virtues of grants from the National Heart, Lung and Blood Institute.

?